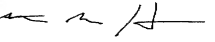
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Wisniewski et al.	**Group Art Unit:**	3743
Serial No.:	10/057,610	**Examiner:**	John K. Ford
Filed:	January 25, 2002	**Appeal No.:**	

Title: FREEZING AND THAWING OF BIOPHARMACEUTICALS WITHIN A VESSEL HAVING A REMOVEABLE STRUCTURE WITH A CENTRALLY POSITIONED PIPE

CERTIFICATE OF ELECTRONIC TRANSMISSION

I hereby certify that this correspondence is being transmitted electronically to: Examiner John K. Ford, Group Art Unit 3744, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on February 28, 2007.



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Date of Signature: February 28, 2007

To: Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Response to Notification of Non-Compliant Appeal Brief and Appellant's Amended Appeal Brief
To the Board of Patent Appeals and Interferences

Dear Sir:

This communication is being filed in Response to the Notification of Non-Compliant Appeal Brief dated February 13, 2007, and supplements the Brief of Appellant filed on June 14, 2004. The one month due date to file a response is March 13, 2007. Accordingly, this response is timely filed.

Real Party In Interest

This application is assigned to **Integrated Biosystems, Inc.** by virtue of an assignment executed on October 1, 1997 by the co-inventors and recorded with the United States Patent and Trademark Office on reel 9068, frame 0033. Therefore, the real party in interest is **Integrated Biosystems, Inc.**

Related Appeals and Interferences

To the knowledge of the appellant, appellant's undersigned legal representative, and the assignee, there are no interferences which will directly affect or be directly affected by or having a bearing on the Board's decision in the instant appeal. There are two other appeals that may be directly affected by or have a bearing on the Board's decision in the instant appeal. All of these appeals involve the same Examiner. These appeals involve the following applications.

Serial Number 08/895,936, notice of appeal filed April 19, 2004.
Serial Number 09/881,909, notice of appeal filed April 19, 2004.

The Board has not issued a decision in either of these appeals. Accordingly, there are no copies of any decisions rendered by a court or the Board in the proceedings identified above to be attached pursuant to 37 CFR 41.37(c)(1)(x).

Status of Claims

This patent application was filed on January 25, 2002 as a continuation application of U.S. Application Serial No. 08/895,936, which is still pending before the U.S. Patent Office before the same Examiner, and which is also being appealed. As filed, the application included nineteen (19) claims, of which two (2) were independent claims (i.e. claims 1 and 6).

In an initial Office Action dated September 9, 2002, claims 1-19 were subject to restriction and election requirement. The Examiner considered the apparatus claims (i.e.

claims 6-19) and the method claims (i.e. claims 1-5) as two distinct inventions. In appellant's response dated October 9, 2002, appellant elected to pursue the method claims, claims 1-5 and newly added method claims 20-29, which include three (3) independent claims, namely claims 1, 20 and 25. In appellant's response dated October 9, 2002, no claims were amended.

In a second Office Action dated February 11, 2003, claims 1-5 and 20-29 were rejected under 35 U.S.C. §112, second paragraph, because the Examiner considered the term "biopharmaceutical product" ambiguous. These same claims were also rejected under 35 U.S.C. §103(a) as being unpatentable over the combined teachings of the 1992 publication by Wisniewski and Wu and the 1986 Kalhori and Ramadhyani article entitled "Studies on heat transfer from a vertical cylinder with or without fins, embedded in a solid phase change medium" and U.S. Patent No. 2,114,642 to West. In appellant's response dated April 14, 2003, claims 1, 20 and 25 were amended to recite that "at least a portion of the central axis of the elongated pipe is positioned coaxially with the central axis of the vessel."

Appellant received a final Office Action dated February 24, 2004 (almost five months after filing its response dated October 7, 2003) repeating the 35 U.S.C. §112, second paragraph, and 35 U.S.C. §103(a) rejections of claims 1-5 and 20-29.

A Notice of Appeal to the Board of Patent Appeals and Interferences was filed on April 19, 2004. The status of the claims is therefore as follows:

Claims allowed:	None
Claims objected to:	None
Claims rejected:	1-5 and 20-29
Claims canceled:	None
Claims withdrawn:	6-19

Appellant is appealing the rejection of claims 1-5 and 20-29.

Status of Amendments

Appellant proffered no response to the final Office Action dated February 24, 2004. The claims as set out in the Appendix include all prior entered amendments.

Summary of the Invention

In one aspect of the invention, as recited in claim 1, a method of preserving a biopharmaceutical product includes placing a medium comprising a biopharmaceutical product (e.g. [0110]) within a vessel (e.g. 4, FIG. 1; [0062]) having a central axis (e.g. FIG. 1) and an interior cavity (e.g. FIG. 1) defined by an interior wall (e.g. 10, FIG. 1; [0062]) of the vessel (e.g. 4, FIG. 1; [0062]); flowing a cooling fluid (e.g. [0064]) through a removably mounted heat exchange structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8) within the interior cavity (e.g. 10, FIG. 1; [0062]) of the vessel (e.g. 4, FIG. 1; [0062]), the structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8; FIG. 16a) comprising an elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) having a central axis (e.g. FIG 1; FIG. 8; FIG. 16; [0103]), wherein at least a portion of the central axis (e.g. FIG 1; FIG. 8; FIG. 16a) of the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) is positioned coaxially with the central axis (e.g. FIG. 1) of the vessel (e.g. 4, FIG. 1; [0062]) within the cavity (e.g. FIG. 1), the structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8) having one or more heat transfer members (e.g. 6, FIG. 1 and [0064]; 80, FIG. 8) thermally coupled thereto; and actively cooling (e.g. [0070]) the interior wall (e.g. 10, FIG. 1; [0062]) using a fluid (e.g. [0070]).

In a further aspect of the invention, the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) is tubular (e.g. FIGs. 1, 8 and 16a) and adapted to be actively cooled using a fluid (e.g. [0064]; [0089]; [0103]). In yet a further aspect of the invention, the one or more of the heat transfer members are fins (e.g. 6, FIG. 1; [0062]; FIG. 8 and [0089]). In yet a further aspect of the invention, the one or more of said fins (e.g. 6, FIG. 1; [0062]; FIG. 8 and [0089]) extend radially from said elongated pipe (e.g. FIG. 1 and FIG. 8)). In yet another aspect of the invention, the vessel (e.g. 4, FIG. 1; [0062])

comprises an open end which is closable by a removable top (e.g. FIG. 1), the structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8; FIG. 16a) being removable (e.g. [0015])through said open end (e.g. FIG. 1) of said vessel (e.g. 4, FIG. 1; [0062]).

In a further embodiment of the invention, as recited in claim 20, Appellant claims a method for facilitating the processing of a biopharmaceutical product comprising providing a vessel (e.g. 4, FIG. 1; [0062]) adapted to receive a medium comprising a biopharmaceutical product (e.g. [0110]) therein, the vessel (e.g. 4, FIG. 1; [0062]) having an interior cavity (e.g. FIG. 1) defined by at least an interior wall (e.g. 10, FIG. 1; [0062]) of the vessel (e.g. 4, FIG. 1; [0062]), the vessel (e.g. 4, FIG. 1; [0062]) having a central axis (e.g. FIG. 1). The method further comprises providing a passage (e.g. 22, FIG. 1; [0070]) for actively cooling the interior wall (e.g. 10, FIG. 1; [0062]) using a cooling fluid (e.g. [0070]). The method further comprises providing a heat exchange structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8) within the cavity (e.g. FIG. 1), the heat exchange structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8) including an elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) having a central axis (e.g. FIGs. 1, 8 and 16a), wherein at least a portion of the central axis (e.g. FIGs. 1, 8 and 16a) of the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) is positioned coaxially with the central axis (e.g. FIGs. 1, 8 and 16a) of the vessel (e.g. 4, FIG. 1; [0062]) within the cavity (e.g. FIG. 1), the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8) having one or more heat transfer members (e.g. 6, FIG. 1 and [0064]; 80, FIG. 8) thermally coupled thereto, the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) defining a passage (e.g. 12, FIG. 1; [0064]; FIG. 8; FIG. 16a) for actively cooling the one or more heat exchange members (e.g. 6, FIG. 1 and [0064]; 80, FIG. 8) using a cooling fluid (e.g. [0070]). In a further aspect of the invention, the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) is tubular (e.g. FIGs. 1, 8 and 16a) and adapted to be actively cooled using a fluid (e.g. [0064]; [0089]; [0103]). In yet a further aspect of the invention, the one or more of the heat transfer members are fins (e.g. 6, FIG. 1; [0062]; FIG. 8 and [0089]). In yet a further aspect of the invention, the one or more of said fins (e.g. 6, FIG. 1; [0062]; FIG. 8 and [0089]) extend radially from said elongated pipe (e.g. FIG. 1 and FIG. 8)). In yet another aspect of the invention, the vessel (e.g. 4, FIG. 1; [0062])

comprises an open end which is closable by a removable top (e.g. FIG. 1), the structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8; FIG. 16a) being removable (e.g. [0015]) through said open end (e.g. FIG. 1) of said vessel (e.g. 4, FIG. 1; [0062]).

In a further embodiment of the invention, as recited in claim 25, Appellant claims a method of processing a biopharmaceutical product comprising providing a vessel (e.g. 4, FIG. 1; [0062]) adapted to receive a medium comprising a biopharmaceutical product (e.g. [0110]) therein, the vessel (e.g. 4, FIG. 1; [0062]) having an interior cavity (e.g. FIG. 1) defined by an interior wall (e.g. 10, FIG. 1; [0062]) of the vessel (e.g. 4, FIG. 1; [0062]) and a heat exchange structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8) within the cavity (e.g. FIG. 1), the heat exchange structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8) having an elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) having a central axis (e.g. FIG. 1), wherein at least a portion of the central axis (e.g. FIG. 1) of the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) is positioned coaxially with the central axis (e.g. FIG. 1) of the vessel (e.g. 4, FIG. 1; [0062]) within the cavity (e.g. FIG. 1), the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8) having one or more heat transfer members (e.g. 6, FIG. 1; [0062]; FIG. 8 and [0089]) thermally coupled thereto; placing a medium comprising a biopharmaceutical product (e.g. [0110]) within the vessel (e.g. 4, FIG. 1; [0062]); actively cooling the interior wall (e.g. 10, FIG. 1; [0062]) using a cooling fluid (e.g. [0070]); actively cooling the heat exchange structure (e.g. 8, FIG. 1 and [0064]; 81, FIG. 8) by flowing a fluid (e.g. [0064]) through the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]); and freezing the medium within the vessel (e.g. 4, FIG. 1; [0062]) to preserve said biopharmaceutical product (e.g. [0110]). In a further aspect of the invention, the elongated pipe (e.g. 12, FIG. 1; 81, FIG. 8; 602, FIG. 16a; [0103]) is tubular (e.g. FIGs. 1, 8 and 16a). In yet a further aspect of the invention, the one or more of the heat transfer members are fins (e.g. 6, FIG. 1; [0062]; FIG. 8 and [0089]). In yet a further aspect of the invention, the one or more of said fins (e.g. 6, FIG. 1; [0062]; FIG. 8 and [0089]) extend radially from said elongated pipe (e.g. FIG. 1 and FIG. 8)). In yet another aspect of the invention, the vessel (e.g. 4, FIG. 1; [0062]) comprises an open end which is closable by a removable top (e.g. FIG. 1), the structure

(e.g. 8, FIG. 1 and [0064]; 81, FIG. 8; FIG. 16a) being removable (e.g. [0015]) through said open end (e.g. FIG. 1) of said vessel (e.g. 4, FIG. 1; [0062]).

Grounds of Rejection to be Reviewed on Appeal

1. Whether the term "biopharmaceutical product" is ambiguous under 35 U.S.C. §112, second paragraph.

2. Whether claims 1-5 and 20-29 were rendered obvious under 35 U.S.C. §103(a) by the combined teachings of the 1992 publication by Wisniewski and Wu ("the 1992 Wisniewski and Wu publication") and the 1986 Kalhori and Ramadhyani article entitled "Studies on heat transfer from a vertical cylinder with or without fins, embedded in a solid phase change medium" ("1986 Kalhori and Ramadhyani article") and U.S. Patent No. 2,114,642 to West ("the '642 patent").

3. Whether appellant satisfied its duty under Rule 56.

Argument

1. The Term "Biopharmaceutical Product" Is Not Ambiguous

As noted, claims 1-5 and 20-29 stand rejected under 35 U.S.C. §112, second paragraph, because the Examiner considered the term "biopharmaceutical product" ambiguous. Reversal of this rejection is respectfully requested.

Appellant did not provide a definition in the specification for the term "biopharmaceutical product." This term has a recognized meaning to those of ordinary skill in the art. The specification provided a number of examples of the type of biopharmaceutical products that may be processed by the present invention. The term "biopharmaceutical product" as set forth in the Specification in paragraph 29 includes, but is not limited to, proteins, cells, antibodies, medicines, plasma, blood, buffer

solutions, viruses, serum, cell fragments, cellular components, and any other biopharmaceutical product.

Appellant also provided a definition of a "biopharmaceutical product" in a previous Amendment dated April 13, 2000 submitted in the parent Application Serial No. 08/895,936 as "a product derived from biological sources that has an intended therapeutic application and whose manufacturing is or will be regulated by pharmaceutical or veterinary regulatory agencies." This definition is supported by the Declarations of Chris J. Burman, V. Bryan Lawlis, Jr., and David A. Vetterlein ("the Declarants"), who are persons of ordinary skill in the art, which the Examiner is fully aware.

Despite support of the aforementioned understanding of the term of "biopharmaceutical products" from three persons of ordinary skill in the art having over 72 years of experience in the biotechnology and biopharmaceutical industry, the Office erroneously complicated the well recognized understanding of this term. For example, the Office sets forth an opinion in concluding that orange juice and milk are biopharmaceutical products. In particular, the Examiner makes an unsupported statement in the final Office Action on page 14 that "[b]lood *would probably* freeze more in the manner of orange juice or milk given its nearly macroscopic cellular nature whereas virus in a suitable buffer solution or water would freeze in the manner of pure or salty water." (emphasis added). Based on such reasoning and unsupported statements, the Office indicates that the definition offered by the Declarants appears to be unworkable. (See page 14 of the Office Action). However, when not defined by an applicant in the specification, the words of a claim must be read as they would be interpreted by those of ordinary skill in the art, MPEP 2111.01, not by the Examiner himself.

In the final Office action, the Examiner also suggests that nothing in the declarations address why one designing freezing equipment for biopharmaceutical products disclosed in the specification would not look to the art of freezing water, orange juice or solids suspended in liquids. To the contrary, this issue has been addressed

numerous times in previous responses and in the specification. As provided in the specification, appellant recognized, among other things, that the apparatus and method according to the aspects of the present invention are suited for use in processing biopharmaceutical products, as that term is understood by those of ordinary skill in the art. For example, the recited apparatus and method promotes uniform freezing at a rapid pace, which allows the biopharmaceutical product in the container to be frozen in as close to its native state as possible. (Specification, paragraph 32). Additionally, the present invention allows the freezing process to be done in a repeatable fashion so that a user can be assured that the freezing process is not causing batch to batch variations in the product. (Specification, paragraph 32).

Appellant respectfully submits that improper processing of biopharmaceutical product by, such as, for example, freezing and thawing, destroys biopharmaceutical products. In contrast, other products, such as, for example, orange juice, milk, water, particulate materials, and comestibles do not have the same processing concerns as biopharmaceutical products. Therefore, such products as orange juice, milk, water, particulate materials and comestibles, which do not require uniform freezing at a rapid pace which allow them to be frozen in as close to its native state as possible in order to prevent damage, are not included in the definition of biopharmaceutical products. In particular, the method or apparatus used to process (e.g. freeze or thaw) these other products is not critical and will not destroy these other products.

Appellant, however, recognizes that, for example, a "buffer solution" can indeed be a biopharmaceutical product depending upon the contents of such a solution. In lab chemistry, buffers are associated with the maintaining of certain pH levels, while biopharma vocabulary (which is relevant to this application) uses the term buffers very broadly, including buffers with proteins (like Human Serum Albumin) or amino acids (multiple amino acids are used, for example, lysine or arginine) clearly having biomolecules which can be damaged by improper freezing. It is readily apparent that buffer solutions which are biologically based may indeed be regulated and be a

biopharmaceutical product. Appellant respectfully submits that if, for example, a particular buffer solution is not derived from biological sources nor regulated by FDA, then it would not be considered a biopharmaceutical product under the aforementioned understanding of the term. The list of potential biopharmaceutical products provided in the specification sets forth examples of products which may be biopharmaceuticals. Because the term has a recognized meaning within the art, it is readily apparent to one of ordinary skill in the art what the term "biopharmaceutical product" means.

Therefore, Appellant respectfully traversed the opinions set forth by the Office in the Office Actions that orange juice, milk, water, comestibles, particulate materials and any other non-biopharmaceutical products (e.g. orange juice and milk) relied upon by the Office Action are considered a biopharmaceutical product and that vessels that freeze such materials are relevant to the delicate preservation of biopharmaceutical products. Appellants also requested the Office to support, by a reference or affidavit pursuant to M.P.E.P. § 2144.04, its position and opinion or in contradiction to the above definition and Declarations by three Declarants of ordinary skill in the art. (See Applicants' Response dated April 13, 2003, page 9). Specifically, appellant requested that the Office show that products such as orange juice, milk and comestibles require uniform freezing at a rapid pace which allow them to be frozen in as close to its native state as possible in order to prevent damage. The Office ignored this request. Instead, the Examiner maintains his rejection and continues to rely on his own personal opinion and knowledge, without providing a supporting reference or affidavit. (See pages 11-13 of the final Office Action).

Appellant respectfully submits that one of ordinary skill in the art is capable of distinguishing and classifying which products are and are not biopharmaceutical products based on the above definition, as evidenced by, for example, the Declarants classification of milk and orange juice as not being pharmaceutical products in their Declarations. For example, one of ordinary skill in the art is capable of determining which proteins, cells, antibodies, medicines, plasma, blood, buffer solutions, viruses, serum, cell fragments,

cellular components, and any other biopharmaceutical product are considered a biopharmaceutical product under the above definition.

Finally, the reliance by the Office in the final Office Action (page 13) on an interpretation of a "would-be infringer" in rejecting the term "biopharmaceutical products" is improper. Under M.P.E.P. § 2173.02, definiteness of claim language must be analyzed in light of the content of the particular application disclosure, the teachings of the prior art and the claim interpretation that would be given *by one possessing the ordinary level of skill in the pertinent art at the time the invention was made.* Appellant respectfully submits that the proper inquire is how "biopharmaceutical product" will be interpreted by a person of ordinary skill in the art, not by a "would be" infringer. Therefore, the Office, in maintaining the rejection of the term "biopharmaceutical products" on this basis, failed to follow this approach.

Accordingly, Appellant respectfully submits that the term "biopharmaceutical product" is definite.

2. Claims 1-5 And 20-29 Are Patentable Over The Combined Teachings Of The 1992 Wisniewski And Wu Publication, The 1986 Kalhori And Ramadhyani Article And The '642 Patent

As noted, claims 1-5 and 20-29 stand rejected under 35 U.S.C. §103(a) as obvious over the combined teaching of the 1992 Wisniewski and Wu Publication, the 1986 Kalhori and Ramadhyani article and the '642 patent.

In support of this rejection, the Office relies on features in the cited prior art that are not recited in the claims. For example, the Office states that the heat exchange members in the 1992 Wisniewski and Wu publication are in "close spaced proximity" to the interior surface of the container. The Office also focuses on the lack of explicit disclosure in this publication of a "thermal bridge of ice", but vigorously argues that such a thermal bridge is inherently formed based on disclosures in other U.S. patents (See

pages 16-20 of the final Office Action). Further, the Office points to both the 1992 Wisniewski and Wu article and the '642 patent to show compartmentation (e.g. fins configured to divide the tank into compartments). However, none of these features relied upon by the Office are recited in any of the independent or dependent claims of the present application. Specifically, none of the claims require the fins to be "in close spaced proximity" to the interior surface of the container or to divide the tank into compartments, or a "thermal bridge of ice". Instead, the appellants invention is directed to a heat exchange structure comprising an elongated pipe being centrally positioned (i.e. coaxially) within the cavity having one or more heat transfer members thermally coupled thereto.

a. The Office Improperly Combined The Cited References

Initially, appellant notes that each of the references relied upon by the Office to reject the claims teach completely different processes to freeze products by using completely different principles. In fact, the cited references teach away from each other and, therefore, there is no motivation or suggestion to combine. Further, aside from the 1992 Wisniewski and Wu publication, none of the cited references disclose biopharmaceutical products or recognize the problems associated with processing such products.

i. The 1992 Wisniewski and Wu Publication

Specifically, the 1992 Wisniewski and Wu publication discloses a device having an internal heat transfer coil pipe with fins welded to the external surface of the coil pipe. The fins attached to the coil are very small and thin and were designed only to aid the freezing around the loop coil in order to increase the relatively small surface area of the loop pipe (e.g. adding more cold surface area). The outside of this device is cooled. A copy of this device is reproduced, for convenience, below:

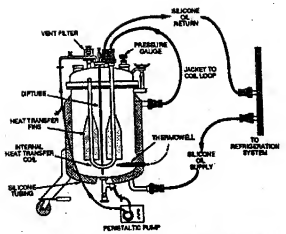

Figure 1. Freeze-thaw Vessel: Thawing Configuration

As shown, the fins attached to the pipe coil are very small and thin and were designed only to aid the freezing around the loop coil in order to increase the relatively small surface area of the loop pipe (e.g. adding more cold surface area). (Second Wisniewski Declaration, ¶8).

ii The 1986 Kalhori and Ramadyani Article

The 1986 Kalhori and Ramadyani article involves the investigation of the solidification of a paraffin[1] in a smooth, thin-walled metal cylindrical tank having an electrical strip heater wrapped around the upper part of the tank. The purpose of the investigation was to demonstrate that natural convection in the liquid phase plays a dominant role in melting and to a certain extent influences freezing. The investigation involves a comparison of the temperature distributions in the paraffin using a plain vertical cylinder in the tank and a vertical cylinder with fins, during cyclic melting and freezing. This cyclic cooling and heating generates convectional currents in the liquid phase of the medium. There is no disclosure or suggestion that the external tank walls are actively cooled. In contrast, the vessel is wrapped with an electrical ban heater to warm the medium from the outside while the cylinder within is cooling it. Therefore, the

[1] Paraffin is a white, waxy, odorless, tasteless solid substance consisting of a mixture of straight chais saturated hydrocarbon used to make, for example, candles, sealing preserving jars, waterproofing paper

temperature closer to the external wall from within the vessel increases, the temperature closer to the cylinder decreases, and heat transfer to the paraffin occurs from the cylinder.

The 1986 Kalhori and Ramadyani article simply concludes that the use of fins works better than no fins. However, this fact was already recognized in the 1992 Wisniewski and Wu publication as shown by the disclosure of the coil pipe having fins attached thereto. There is absolutely no disclosure or suggestion in the 1986 Kalhori and Ramadyani article of biopharmaceutical product or a discussion or recognition of the problems associated with processing biopharmaceutical product. Therefore, there is no motivation or suggestion to combine the 1986 Kalhori and Ramadyani article with the 1992 Wisniewski and Wu article because the 1986 Kalhori and Ramadyani article does not involve, or recognize the problems associate with processing, biopharmaceutical products.

There is also no motivation to combine the interior structure disclosed in the 1986 Kalhori and Ramadyani article with the container disclosed in the 1992 Wisniewski and Wu publication because the devices disclosed in both articles involve different principles of freezing. Specifically, the device disclosed in the 1992 Wisniewski and Wu article cools the container from the outside and the inside and the 1986 Kalhori and Ramadyani article heats the container on the outside while cooling the container inside. Therefore, contrary to the Examiner's suggestion, it would not be obvious to simply put the finned cylinder disclosed in the 1986 Kalhori and Ramadyani article in the tank disclosed in the 1992 Wisniewski and Wu publication because one of ordinary skill in the art would not be motivated to look towards the 1986 Kalhori and Ramadyani article to combine with the 1992 Wisniewski and Wu publication due to problems associated with processing biopharmaceutical products and the fact that the device in the 1992 Wisniewski and Wu article already uses fins and cools the device from the inside using the coil pipe.

In support of this combination, the Office simply concludes that it would be obvious to one of ordinary skill in the art to replace the heat exchanger and fins of the

1992 Wisniewski and Wu publication with the heat exchanger and fins shown in the 1986 Kalhori and Ramadhyani article to improve heat transfer and to facilitate ease of construction as well as to facilitate easy removal from the frozen mass. However, the Office fails to explain how substituting one structure for another in a vessel using completely different principles would produce the same desirable freezing results of biopharmaceutical products, especially in view of the Examiner's own statements on page 3 in the final Office Action dated February 24, 2004 that:

> It is respectfully submitted that these freezing phenomena are so complex that no human being including one with nearly 30 years of experience can accurately predict such results. Purporting to have such ability only diminishes ones credibility.

iii. The '642 Patent

The '642 patent is directed to the acceleration of the production of frozen articles such as milk, sherbet and similar substances, not to the preservation of biopharmaceutical products. The '642 patent describes freezing that prevents sugar deposition form the original solution. The object of this patent is not to optimize the preservation of biopharmaceutical products by freezing, but rather to fast freeze to make milk and sherbet look a certain way (e.g appealing to consumers). In the '642 patent, liquid refrigerant gets to the header (3) where it boils in cup (15) onto which the container with product (8) is slipped. Since the refrigerant boils inside the cups (15), then there is no control of freezing (e.g. very fast freezing, see page 2, lines 60-66). Contrary to the Office's statements, the '642 patent does not show any cooling surface extensions such as fins or an elongated pipe.

iv. No Motivation To Combine

Therefore, the 1992 Wisniewski and Wu publication, the 1986 Kalhori and Ramadyani article and the '642 West patent each freeze products by completely different ways using completely different freezing principles. As such, these references teach

away from each other and there is simply no motivation to combine the same. Specifically, the 1986 Kalhori and Ramadyani article teaches heating the medium from the outside of the cylinder while the structure within was cooling it. In sharp contrast, the 1992 Wisniewski and Wu publication teaches cooling the outside and inside of the cylinder. Finally, the '642 West patent discloses a method of freezing completely different from the device in the 1992 Wisniewski and Wu publication and the 1986 Kalhori and Ramadyani article. Appellant respectfully submits that one of ordinary skill in the art would not look towards a device that is heated on the outside to combine with a device that was cooled on the inside because the methods and principles of freezing used in both devices are completely different. This conclusion is reinforced by statements made by this same Examiner in the final Office Action of the parent application (Serial No. 08/895,936) highlighting the difficulty in determining the temperature distribution of these types of devices. These statements include the following:

> The Examiner . . . does not believe that there is anyone who can model or calculate these temperature profiles without the aid of sophisticated computers and/or experimental work. . . .The processes of modeling natural convection and moving-front phase change occurring together with sub-cooling is, to the Examiner's knowledge, is state of the art or beyond the state of the art in numerical solutions on computers. See Final Office Action in Serial No. 08/895,936, page 8.

> It is respectfully submitted that these freezing phenomena are so complex that no human being including one with nearly 30 years of experience can accurately predict such results. Purporting to have such ability only diminishes ones credibility. See Final Office Action in Serial No. 08/895,936, page 10.

> Thus, researchers, other than Mr. Wisniewski, state that accurate modeling of phase change heat transfer in tanks with finned element such as shown in Figure 3 of the K&R article can only be done by computers or by direct empirical measurement. See Final Office Action in Serial No. 08/895,936, page 11.

> [T]he temperature distribution must either be measured or generated by very sophisticated computer programs, which have had their validity checked against measured data. See Final Office Action in Serial No. 08/895,936, page 12.

> Mr. Wisniewski's guesswork even in declarative form is simply no substitute for real evidence. Neither he nor any other person on the planet is in a position to properly guess at the actual temperature distribution. See Final Office Action in Serial No. 08/895,936, page 14.

Accordingly, the Office admits that even those of ordinary skill in the art cannot look at and simply combine the cited references and arrive at the desired result disclosed in the Specification and recited in the claims of the present invention without experimentation or the aid of a computer. Therefore, there is simply no suggestion or motivation to combine the structure within the 1986 Kalhori and Ramadyani article with the cooled cylinder of the Genentech device.

The Office in its final Office Action ignored appellant's argument set forth in appellant's response dated April 14, 2003, and repeated above, concerning the different methods of freezing products disclosed in these cited references using completely different principles. Since the Office Action failed to address these arguments, appellant respectfully submits that this deficiency at least renders incomplete a rejection based on an alleged combination of the cited references. For at least this reason, reversal of the obviousness rejection and allowance of the claims are respectfully requested.

b. The Cited References Do Not Disclose The Recited Method

Appellant's independent claims recite: "said structure comprising an elongated pipe having a central axis, wherein at least a portion of the central axis of said elongated pipe is positioned coaxially with the central axis of the vessel within said cavity." Appellant's independent claims also require active cooling of the interior wall of the vessel.

The 1992 Wisniewski and Wu publication fails to teach or suggest appellants' claimed element of an elongated pipe positioned coaxially with a central axis of the vessel. The Office concedes this in the final Office Action on page 15 by stating that this publication "lacks a 'spur tube' type cooler in the center. The 1986 Kalhori and

Ramadyani article fails to disclose active cooling of the exterior wall of the vessel. In contrast, the device in this article heats the exterior wall. Finally, as explained above, the '642 patent describes a completely different apparatus and method for freezing non-biopharmaceutical products.

Therefore, in view of the reasons provided above, the 1992 Wisniewski and Wu publication, the 1986 Kalhori and Ramadyani article, and the '642 patent fails to disclose each and every limitation recited in the claims and there is no motivation or suggestion to combine these references.

3. Appellant Satisfied Their Duty Under Rule 56

In the second Office Action dated February 11, 2003, the Examiner requested additional information concerning the prior art devices disclosed in the specification and the Genentech device disclosed in the 1992 disclosure of Wisniewski and Wu. The Examiner also suggested that the inventors contact Genentech to obtain the dimensions of the prior art Genentech device. However, the Examiner incorrectly assumed that the appellants were in possession of this information because they worked on the Genentech device more than a decade ago.

In appellant's response dated April 14, 2003, appellant made clear to the Examiner that the applicants do not work for Genentech and were not in possession of the 1992 Genentech device. In an effort to further assist the Office, one of the inventors, Mr. Wisniewski, submitted a Second Declaration that provided as much information that he could remember concerning the Genentech device.

In a third Office Action dated September 30, 2003, the Examiner considered appellant's response dated April 14, 2003 as not fully responsive to the second Office Action because the appellant failed to provide a copy of the first and second declarations of Mr. Wisniewski. The Examiner also suggested that applicants submit a third declaration to explain why they did not contact Genentech.

Appellant promptly filed a response on October 7, 2003 by submitting a copy of the first and second declarations and explaining that they have disclosed as much information as they can remember concerning the prior art, especially the Genentech device. Therefore, appellant has satisfied their duty under Rule 56 and the Office should have considered appellant's response to the third Office Action as a complete reply under 37 C.F.R. §1.105(a)(3).

In the final Office Action, the Examiner provides his personal response to each paragraph in the declarations submitted by Mr. Wisniewski. However, these declarations were not submitted to support the claims in the present application, but rather to contest the Examiner's accusations that appellant failed to provide information concerning the prior art, specifically the Genentech device disclosed in the 1992 Wisniewski and Wu article. A response to the Examiner's position concerning the substance of these declarations is not necessary at this point in time because, as mentioned above, the claims in the present application do not recite a "thermal bridge" or a relationship (in distance) between the fins and interior wall of the vessel.

Appellant provided the Office with as much information concerning the prior art that is presently know or readily available. Whether or not Genentech is a competitor or customer (both are actually true), Rule 56 does not require an applicant to contact another company for a competitive device in order to conduct experiments using its own equipment to perform testing to support the Examiner's unsupported beliefs and speculation, which have no bearing upon the claims. Clearly, this request exceeds the requirement under Rule 56.

Therefore, appellant submits that all information that is known and readily available was submitted.

Conclusion

For the reasons set forth above, reversal of the rejections and allowance of this application are respectfully requested.

Dated: February 28, 2007

Respectfully submitted,

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APPENDIX

CLAIMS FOR APPLICATION SERIAL NUMBER 10/057,610

1. A method of preserving a biopharmaceutical product comprising:

placing a medium comprising a biopharmaceutical product within a vessel having an interior cavity defined by an interior wall of said vessel, said vessel having a central axis;

flowing a cooling fluid through a removably mounted heat exchange structure within said interior cavity of said vessel, said structure comprising an elongated pipe having a central axis, wherein at least a portion of the central axis of said elongated pipe is positioned coaxially with the central axis of the vessel within said cavity, said structure having one or more heat transfer members thermally coupled thereto; and

actively cooling said interior wall using a fluid.

2. The method of claim 1, wherein said elongated pipe is tubular and adapted to be actively cooled using a fluid.

3. The method of claim 1, wherein said one or more of said heat transfer members are fins.

4. The method of claim 3, wherein said one or more of said fins extend radially from said elongated pipe.

5. The method of claim 1, wherein said vessel comprises an open end which is closable by a removable top, said structure being removable through said open end of said vessel.

20. A method for facilitating the processing of a biopharmaceutical product comprising:

providing a vessel adapted to receive a medium comprising a biopharmaceutical product therein, said vessel having an interior cavity defined by at least an interior wall of said vessel, said vessel having a central axis;

providing a passage for actively cooling said interior wall using a cooling fluid; and

providing a heat exchange structure within said cavity, said heat exchange structure including an elongated pipe having a central axis, wherein at least a portion of the central axis of said elongated pipe is positioned coaxially with the central axis of the vessel within said cavity, said elongated pipe having one or more heat transfer members thermally coupled thereto, said elongated pipe defining a passage for actively cooling the one or more heat exchange members using a cooling fluid.

21. The method of claim 20, wherein said elongated pipe is tubular and adapted to be actively cooled using a fluid.

22. The method of claim 20, wherein said one or more of said heat transfer members are fins.

23. The method of claim 22, wherein said one or more of said fins extend radially from said elongated pipe.

24. The method of claim 20, wherein said vessel comprises an open end which is closable by a removeable top, said structure being removeable through said open end of said vessel.

25. A method of processing a biopharmaceutical product comprising:

providing a vessel adapted to receive a medium comprising a biopharmaceutical product therein, said vessel having an interior cavity defined by an interior wall of said vessel and a heat exchange structure within said cavity, said heat exchange structure having an elongated pipe having a central axis, wherein at least a portion of the central axis of said elongated pipe is positioned coaxially with the central axis of the vessel within said cavity, said elongated pipe having one or more heat transfer members thermally coupled thereto;

placing a medium comprising a biopharmaceutical product within said vessel;

actively cooling said interior wall using a cooling fluid;

actively cooling said heat exchange structure by flowing a fluid through the elongated pipe; and

freezing the medium within said vessel to preserve said biopharmaceutical product.

26. The method of claim 25, wherein said elongated pipe is tubular.

27. The method of claim 25, wherein said one or more of said heat transfer members are fins.

28. The method of claim 27, wherein said one or more of said fins extend radially from said elongated pipe.

29. The method of claim 25, wherein said vessel comprises an open end which is closable by a removeable top, said structure being removeable through said open end of said vessel.

Evidence Appendix

1) Declaration of Chris J. Burman – This declaration was entered and considered by the Examiner in the Office Action dated February 11, 2003.

2) Declaration of V. Bryan Lawlis, Jr. - This declaration was entered and considered by the Examiner in the Office Action dated February 11, 2003.

3) Declaration of David A. Vetterlein - This declaration was entered and considered by the Examiner in the Office Action dated February 11, 2003.

4) Declaration of Richard Wisniewski – This declaration was entered and considered by the Examiner in the Office Action dated February 11, 2003.

5) Second Declaration of Richard Wisniewski - This declaration was entered and considered by the Examiner in the Office Action dated February 11, 2003.

Related Proceedings Appendix

NONE

The Board has not issued a decision in either of the appeals identified above in the Section entitled "Related Appeals and Interferences."